

## **REMARKS**

### **Formal Matters**

Claims 12-14, 16, 18-23, 25, 27-30 and 37-45 are pending after entry of the amendments set forth herein.

Claims 12, 13, 18-21, 25, 27-30 and 37-40 were examined. Claims 12, 13, 18, 19, 21, 28, 29 and 37-40 were rejected. Claims 20, 25, 27 and 30 were objected to.

Claims 12, 19, 25 and 27-29 and 37-40 are amended and claims 41-45 are new. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. Support for the amendments and new claims is found in the claims as originally filed, and throughout the specification, in particular at the following exemplary locations: paragraphs 12, 15, 66, 74 123 and 175. Accordingly, no new matter is added.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

### **Interview summary**

The Applicants wish to express their gratitude to Examiners Whiteman and Voitach for the telephone interview conducted on May 19, 2004, with Applicants' representative James Keddie, Carol Francis and Michael German. The outstanding rejections were discussed, as well as arguments to overcome those rejections. It was agreed that the only outstanding rejections are under §112, ¶1 with respect to the enablement with respect to the cell to be used in the claimed methods, and under §112, ¶2 with respect to the phrase "gastrointestinal organ cell".

Two publications, Schwitzgebel *et al.* (Development 2000 127:3533-3542) and Vetere (Biochem. J. 2003 371:831-841), were discussed in the context of the outstanding enablement rejection. Those publications are included with those cited in Information Disclosure Statement filed herewith.

Applicants agreed to cancel subject matter relating to embryonic stem cells and discuss what is meant by the term "gastrointestinal organ" in order to expedite allowance of the claims.

### **Information Disclosure Statement**

An Information Disclosure Statement, including a Form PTO/SB0/8A and copies of the references cited therein, is submitted herewith. Applicants would be grateful if the Examiner could initial and return the initialed copy of form PTO/SB0/8A indicating that the references have been considered and made of record.

### **The Response in General**

Subject matter relating to embryonic stem cells has been cancelled from the claims.

For the record, the Applicants define that gastrointestinal organ cells as cells from gastrointestinal organs derived from endoderm, rather than mesoderm or ectoderm. Gastrointestinal organs derived from endoderm include those of the gut tube as well as the associated exocrine glands and ducts that are embryologically derived from the gut tube. Cells from organs derived from mesoderm and ectoderm are not encompassed by the claims.

### **Allowable subject matter**

Applicants note with gratitude the Examiner's indication that claim 30, directed to use of a bHLH neuroendocrine transcription factor and an adult pancreatic cell for production of an insulin-producing cell *in vitro*, is objected to as depending upon a rejected claim, but is otherwise allowable. Applicants

Applicants further note that claims 37-40 are rejected solely under 35 U.S.C. § 112, second paragraph, as being indefinite.

### **Sequence Listing**

The Office Action indicates that SEQ ID NO:20 is listed in the specification in Figure 19A but not listed in the CRF.

A substitute Sequence Listing is filed herewith. The Applicants respectfully request entry of the substitute Sequence Listing.

**Election/Restriction**

Claims 14, 16, 22 and 23 are withdrawn

Applicants note that claims 14, 16, 22 and 23 are withdrawn because they are directed to neuroendocrine transcription factors other than *ngn3*, the species of neuroendocrine transcription factor elected for initial examination.

These withdrawn claims are dependent on generic claims 12 and 19. Pursuant to the instructions set forth in MPEP §809.02(c), claims 14, 16, 22 and 23 should be rejoined with claims 12 and 19 upon allowance of claim 12 and 19.

Accordingly, the Applicants respectfully request rejoinder of claim 14, 16, 22 and 23 if claims 12 and 19 become allowable.

**Claim objections**

Claims 19, 25, 27-29 are objected to for reciting the phrase “said introducing providing”, which the Office believes is a grammatically incorrect phrase.

Without acquiescing to the correctness of this rejection, claims 19, 25, 27-29 have been amended to recite the phrase “wherein said introducing provides for”. The Applicants respectfully submit that the phrase “wherein said introducing provides for” is grammatically correct, and, as such, this objection may be withdrawn.

Claims 20-23, 38 and 40 are objected to because they depend on claim 19. However the Office Action does not indicate what aspect of claims 20-23, 38 and 40 renders their dependency on claim 19 objectionable.

Since claims 20-23, 38 and 40 appear to the Applicants to be appropriately dependent on claim 19, the Office is respectfully requested to provide a specific indication of the defect of these claims

In the absence of a specific indication of the defect of these claims, withdrawal of this objection is respectfully requested.

**Rejection of claims under 35 U.S.C. § 112, first paragraph**

Claims 12, 13, 18, 19, 21, 28 and 29 remain rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which is not described in the specification in such a way as to enable one

skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Specifically, the Office asserts that while the specification is enabling for methods involving pancreas and liver cells, the specification is not enabling for methods embryonic stem cells or cells from other gastrointestinal organs. The Applicants respectfully traverse this rejection.

Without any intention to acquiesce to the correctness of this rejection and solely to expedite prosecution, reference to embryonic stem cells have been cancelled from the claims.

During the aforementioned interview, the Applicants representatives presented factual evidence in the form of two papers published in internationally recognized, peer-reviewed journals (Schwitzgebel *et al.* 2000 and Vetere *et al.* 2003; see attached IDS), supporting their assertion that the subject methods could be used with a wide variety of different cell types. The Examiners indicated that this evidence was sufficient to support the methods recited in the currently pending claims, and, accordingly, this rejection is believed to have been addressed. While PDX1 and HNF3 $\beta$  may be required for endogenous Ngn3 expression in a wild-type cell, this requirement is avoided when recombinant Ngn3-encoding nucleic acid is introduced into the cell.

Withdrawal of this rejection is respectfully requested.

**Rejection of claims under 35 U.S.C. § 112, second paragraph**

Claims 37-40 are rejected under 35 U.S.C. 112, second paragraph, as indefinite for reciting the term “said gastrointestinal organ” for which there is assertedly no antecedent support in the claim.

Without any intent to acquiesce to this rejection, the claims have been amended to recite “said cultured gastrointestinal organ cell”.

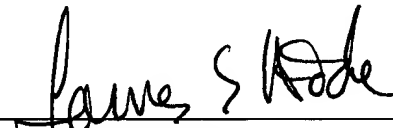
In view of the foregoing discussion, the Applicants respectfully submit that this rejection may be withdrawn.

**SUMMARY**

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCSF-129CIP.

Respectfully submitted,  
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Date: June 15, 2004

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Attachments: Substitute sequence listing  
Information Disclosure Statement

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